Effect of Bailing capsule combined with ethinylestradiol and cyproterone acetate and metformin on lipid metabolism and insulin resistance in patients with polycystic ovary syndrome

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ABSTRACT

Objective: To investigate the effect of Bailing capsule combined with ethinylestradiol and cyproterone acetate and metformin on lipid metabolism and insulin resistance in patients with polycystic ovary syndrome (PCOS). Methods: A total of 108 patients with PCOS who were treated in our hospital between November 2014 and April 2017 were reviewed and divided into routine group (n=67) who received routine therapy and Bailing capsule group (n=41) who received Bailing capsule combined with routine therapy. Routine group received ethinylestradiol and cyproterone acetate and metformin therapy, and Bailing capsule group were treated with Bailing capsule combined with ethinylestradiol and cyproterone acetate and metformin therapy. The differences in the levels of lipid metabolism, insulin resistance indexes as well as inflammatory factors were compared between the two groups before and after treatment. Results: There was no statistically significant difference in serum levels of lipid metabolism, insulin resistance-related indexes and inflammatory factors between the two groups before treatment. After treatment, serum HDL-C content of Bailing capsule group was higher than that of routine group whereas LDL-C and TC contents were lower than those of routine group; serum insulin resistance-related indexes FINS and HOMA-IR levels were lower than those of routine group; serum inflammatory cytokines IL-6, TNF-α, APN and LEP contents were lower than those of routine group. Conclusion: Bailing capsule combined with ethinylestradiol and cyproterone acetate and metformin therapy can effectively improve the lipid metabolism level and inhibit the insulin resistance in patients with PCOS.

1. Introduction

Polycystic ovary syndrome (PCOS) is a common endocrine and metabolism abnormality in women of childbearing age, which is clinically characterized by chronic anovulation and hyperandrogenism, is specifically manifested as irregular menstruation, polytrichia and acne, infertility, etc., and seriously influences women's physical and mental health[1–3]. Ethinylestradiol and cyproterone acetate is a traditional method for the treatment of patients with PCOS, which can protect the endometrium, regulate menstrual cycle and improve the polytrichia and acne caused by hyperandrogenism[4]; metformin is used to improve the insulin resistance in patients with PCOS, and the combination of the two drugs has become a routine method for the treatment of patients with PCOS[5]. Bailing capsule is made from cordyceps sinensis strains under low-temperature fermentation, it has multiple functions such as reducing lipid and glucose, protecting the liver and kidney function and regulating endocrine cooperation, and current research has pointed out that Bailing capsule combined with Diane-35 is better than Diane-35 alone in stimulating ovulation, so some scholars suggest Bailing capsule for adjuvant treatment of PCOS. In this study, Bailing capsule was used together with ethinylestradiol and cyproterone acetate and metformin for the treatment of patients with PCOS, and the effect of the therapy on the patients' condition was discussed.
2. Information and methods

2.1 Case information

A total of 108 patients with PCOS were treated in our hospital between November 2014 and April 2017, and they were reviewed and divided into routine group (n=67) who received routine therapy and Bailing capsule group (n=41) who received Bailing capsule combined with routine therapy. Routine group were 22-35 years old, and the course of PCOS was 1-8 years; Bailing capsule group were 23-37 years old, and the course of PCOS was 2-8 years. The differences in the distribution of age and PCOS course were not significant between the two groups and the study was approved by the hospital ethics committee.

Inclusion criteria: (1) in line with clinical diagnostic criteria for PCOS; (2) n≤40 years old; (3) signing the informed consent form themselves; (4) receiving regular treatment and never quitting in midway. Exclusion criteria: (1) combined with chocolate cyst, premature ovarian failure and other ovarian disorders; (2) with history of ovarian surgery; (3) combined with adnexitis; (4) combined with allergy to any one of Bailing capsule, ethinylestradiol and cyproterone acetate and metformin.

2.2 Therapy

Routine group received ethinylestradiol and cyproterone acetate and metformin treatment, specifically as follows: taking ethinylestradiol and cyproterone acetate tablets orally from the 5 d of menstruation, 1 tablet/time for continuous 21 d, and starting the next course of treatment from the 5 d of withdrawal bleeding. Metformin tablets were taken orally, 1 time/d, 3 times/d (taken orally 30 min before each meal) for 3 months in a row.

Bailing capsule group received Bailing capsule combined with ethinylestradiol and cyproterone acetate and metformin treatment, specifically as follows: Bailing capsule, taken orally, 2 g/time, 3 times/d, taken with ethinylestradiol and cyproterone acetate tablets, for consecutive three courses of treatment. The dosage and usage of ethinylestradiol and cyproterone acetate and metformin were the same as those of routine group.

2.3 Observation indexes

Before and after treatment, fasting cubital venous blood was collected from the two groups to separate the upper serum for test. Automatic biochemical analyzer was used to detect the serum levels of lipid metabolism indexes, including high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) and total cholesterol (TC); chemiluminescent immunoassay was used to measure the serum level of fasting insulin (FINS) and further calculate the insulin resistance index (HOMA-IR); enzyme-linked immunosorbent assay kits were used to detect the serum levels of inflammatory factors interleukin-6 (IL-6), tumor necrosis factor (TNF-α), adiponectin (APN) and leptin (LEP).

2.4 Statistical processing

Lipid metabolism indexes, insulin resistance-related indexes and inflammatory factors were all input in SPSS 26.0, P value was calculated and P<0.05 was set as the standard of statistical significance in differences.

3. Results

3.1 Lipid metabolism index contents

Comparison of serum lipid metabolism indexes HDL-C, LDL-C and TC contents between two groups of patients was as follows: before treatment, serum HDL-C, LDL-C and TC contents were not significantly different between the two groups (P>0.05). After treatment, serum HDL-C contents of both groups were higher than those before treatment whereas LDL-C and TC contents were lower than those before treatment; serum HDL-C content of Bailing capsule group was higher than that of routine group whereas LDL-C and TC contents were lower than those of routine group (P<0.05), shown in Table 1.

3.2 Insulin resistance-related indexes

Comparison of serum insulin resistance-related indexes FINS (mU/L) and HOMA-IR levels between two groups of patients was as follows: before treatment, serum FINS and HOMA-IR levels were not significantly different between the two groups (P>0.05). After treatment, serum FINS and HOMA-IR levels of both groups were lower than those before treatment; serum FINS and HOMA-IR levels of Bailing capsule group were lower than those of routine group (P<0.05), shown in Table 2.
for PCOS has gradually attracted attention. Treatment of PCOS, and the application value of Bailing capsule has pointed out that it can be used together with Diane-35 for the treatment of diseases such as nephritis and asthma, current research has shown that it can be used for the treatment of hyperlipidemia in patients with PCOS, which is on the one hand, associated with the direct effect of Bailing capsule on regulating lipid metabolism, and on the other hand, related to its effect on relieving the hyperandrogenism and reducing the lipid metabolism disorders caused by hyperandrogenism.

3.3 Inflammatory factors

Comparison of serum inflammatory factors IL-6 (pg/mL), TNF-α (pg/mL), APN (ng/mL) and LEP (ng/mL) contents between two groups of patients was as follows: before treatment, serum IL-6, TNF-α, APN and LEP contents were not significantly different between the two groups (P>0.05). After treatment, serum IL-6, TNF-α, APN and LEP contents of both groups were lower than those before treatment; serum IL-6, TNF-α, APN and LEP contents of Bailing capsule group were lower than those of routine group (P<0.05), shown in Table 3.

4. Discussion

PCOS is a common female endocrine disease, oral contraceptive ethinylestradiol and cyproterone acetate and insulin sensitiser metformin are the common drugs for it, they are used to adjust the menstrual cycle, improve the insulin resistance, lower testosterone levels, etc. respectively, and they have certain effect on optimizing patients’ condition[6,7]. TCM has attributed the PCOS to "amenorrhoea", "infertility" and other categories, the liver stasis, spleen deficiency, phlegmatic hygrosis, blood stasis and so on are closely related to the development of PCOS, and the treatment should focus on invigorating spleen and nourishing the kidney as well as reducing phlegm and removing blood stasis. Bailing capsule is from cordyceps sinensis strains after low-temperature fermentation, it has the effects such as tonifying kidney, protecting β cells to secrete insulin and aggravate IR; (3) insulin gene mutation; (4) the intracellular signaling transmission process is abnormal after the combination between insulin and receptor[13–15]. The improvement of patients with PCOS is not only manifested as the increased regularity of ovulation, but also manifested as decrease in IR, so the levels of IR-related indicators could quantitatively and objectively reflect the condition of PCOS[16,17]. The results of this study showed that compared with those before treatment, serum FINS and HOMA-IR levels of both groups were decreased after treatment; further compared with those of normal group, serum HDL-C content of Bailing capsule group was higher while LDL-C and TC contents were lower after treatment, indicating that adding Bailing capsule in overall treatment can effectively reduce the degree of hyperlipidemia in patients with PCOS, which is on the one hand, associated with the direct effect of Bailing capsule on regulating lipid metabolism, and on the other hand, related to its effect on relieving the hyperandrogenism and reducing the lipid metabolism disorders caused by hyperandrogenism.

Insulin resistance (IR) plays a vital role in the occurrence and development of PCOS, and the causes of IR specifically include the following: (1) the insulin receptors on cell membrane of the obese decrease relatively, and the sensitivity to insulin declines; (2) the increase of androgen can stimulate the islet β cells to secrete insulin and aggravate IR; (3) insulin gene mutation; (4) the intracellular signaling transmission process is abnormal after the combination between insulin and receptor[13–15]. The improvement of patients with PCOS is not only manifested as the increased regularity of ovulation, but also manifested as decrease in IR, so the levels of IR-related indicators could quantitatively and objectively reflect the condition of PCOS[16,17]. The results of this study showed that compared with those before treatment, serum FINS and HOMA-IR levels of both groups were decreased after treatment; further compared with those of normal group, serum FINS and HOMA-IR levels of Bailing capsule group were lower after treatment, it indicates that Bailing capsule combined with ethinylestradiol and cyproterone acetate and metformin treatment can effectively reduce the IR rate in the patients, and this is one of the important mechanisms for it to improve PCOS.

Current study has shown that IR is a chronic subclinical inflammatory process, and various inflammatory factors participate in IR formation and aggravation process. IL-6 can promote insulin synthesis and cause hyperinsulinemia, and the specific mechanisms include lowering the degree of IRS-1 tyrosine phosphorylation, hindering the insulin signal transduction, cutting GLUT-4 gene transcription, decreasing the insulin-stimulated glucose transport capacity and resulting in IR[18]. TNF-α is one of the factors most
both directly act on the islet β cells and induce IR\[19,20\]. In this study, the contents of above inflammatory factors were compared between the two groups, and it was found that compared with those before treatment, serum IL-6, TNF-α, APN and LEP contents of both groups decreased after treatment; further compared with those of routine group, serum IL-6, TNF-α, APN and LEP contents of Bailing capsule group were low after treatment, it confirms that adjuvant Bailing capsule therapy can effectively inhibit the micro-inflammatory state in patients with PCOS, and this is the inner way for it to inhibit IR.

The adjuvant Bailing capsule therapy can effectively reduce the lipid metabolism disorder and IR degree in patients with PCOS, and the specific mechanism is directly related to its effect on alleviating the micro-inflammatory state in the patients. Bailing capsule is expected to be an important Chinese patent medicine to improve PCOS, and it is worth popularization and application in future clinical practice.

References


